Scientific Abstract

Replication deficient adenovirus (Ad) vectors are being used in a number of human gene therapy strategies to transfer genes *in vivo* for therapeutic purposes. One major hurdle to the effective used of these vectors is the immune host defenses that respond to *in vivo* vector administration with antibodies against the vector and cellular immune process directed toward cells infected with the vector. The purpose of this protocol is to characterize the local (skin), systemic (blood), and distant compartment (lung) immunity in normal individuals after intradermal administration of a replication deficient Ad5-based vector carrying the gene coding for the *E. coli* enzyme cytosine deaminase (CD) (Ad_{GV}CD.10). Following intradermal administration of the Ad_{GV}CD.10 vector to normal individuals, the skin, blood, and lung immune responses to the Ad vector and CD transgene will be evaluated over time. This vector has been safely administered 10 times to 5 individuals with colon carcinoma with no adverse effects (Rockefeller University Hospital Institutional Review Board and Biosafety Committee RCR-163-0696, Recombinant Advisory Committee #9509-125 and Food and Drug Administration BB-IND 6442). This protocol will yield insights into normal human immune responses to both the Ad vector, as well as to a heterologous (i.e., non-human) gene product (CD). Because CD is not a human gene, and humans have no analogous genes, there is no safety risk to evoking immunity against CD, i.e., the study is equivalent to a vaccination study.